Please replace paragraph 33 on page 9 with the following amended paragraph:

Figure 13 illustrates the effect of the LXR pan-agonist Compound 1 on cholesterol efflux in peritoneal macrophages isolated from wildtype (mixed and C57BL/6), LXRα-/- (C57BL/6), LXRβ-/-, and LXRαβ-/- mice. Peritoneal macrophages were cultured *in vitro* for 24 hours, cells were labeled with ^{14}C-cholesterol and cultured for an addition 24 hours in the absence (white bars) or presence (hatched bars) of 1.0 μM Compound 1 to measure cholesterol efflux. Data is expressed as fold induction by Compound 1 (+Compound 1/Vehicle, hatched bars). The value for vehicle treated cells in each group was set at 1.0 (white bars). Data is the average of three samples per group assayed in triplicate. *Signifies that the value is statistically different from the wildtype control value.

REMARKS

The amendments to the specification provide separate descriptions for the individual parts of multiple-part figures and are supported by the text of the specification and the informal figures. No new matter has been added.

Drawings

A set of formal drawings has been submitted under separate cover. A copy of the formal drawings is included herein as Exhibit B for the Examiner's convenience.

Restriction Requirement Under 35 U.S.C. § 121

The Office has requested a restriction to one of the following inventions under 35 U.S.C. § 121: Group I (claims 1-3), drawn to a method for elevating the plasma level of high density lipoprotein (HDL) in a mammal, comprising administering an HDL-elevating LXRβ selective agonist; Group II (claim 4), drawn to a method of decreasing the absorption of dietary cholesterol in the intestine of a mammal, comprising administering an absorption-decreasing

LXRβ selective agonist; Group III (claims 5 and 6), drawn to a method of elevating HDL-associated gene expression in a cell, comprising administering an LXRβ selective agonist to the cell; Group IV (claims 7-9), drawn to a method of decreasing the plasma level of low density lipoprotein (LDL) in a mammal, comprising administering an LDL-decreasing LXRβ selective agonist; Group V (claims 10-12), drawn to a method of identifying an LXRβ selective agonist by testing the candidate compound in a cell-based or biochemical assay; Group VI (claims 13-26), drawn to a method for treating a metabolic disease in a mammal, comprising administering an LXRβ selective agonist; or Group VII (claims 27-28), drawn to a method of identifying an LXRα selective agonist by testing the candidate compound in a cell-based or biochemical assay. Applicants hereby elect Group VI (claims 13-26), without traverse.

With the election of Group VI, the Office further requested the selection of "one disease from claim 14, 20, 21, or 24." The Office also requested the selection of "one additional active agent from the claim 16, 23, or 26." According to the Office, "[t]his is not species election."

It was not clear to Applicants whether the Office seeks the selection of a single disease and single additional active agent for all of the claims or the selection of a single disease or single agent for each of the designated claims. Therefore, Applicants have provided selections for either alternative. If a single disease and single additional active agent is to be selected for claims 13-26, Applicants select diabetes as the disease and thiazolidinedione as the additional active agent. If a single disease or a single additional agent per claim is to be selected, Applicants select diabetes as the disease in claims 14 and 21, and hyperglycemia as the disease from claim 20. Applicants select insulin as the additional active agent of claim 16, thiazolidinedione as the additional active agent of claim 23, and amylin as the additional active agent of claim 26.

Applicants expressly reserve their right under 35 U.S.C. § 121 to file a divisional application directed to the nonelected subject matter during the pendency of this application, or an application claiming priority from this application.

Applicants request examination of the elected subject matter on the merits.

Attached hereto is a marked-up version of the changes made to the specification by the current amendment. In the unlikely event that the transmittal letter is separated from this document and the Patent Office determines that an extension and/or other relief is required, Applicant petitions for any required relief including extensions of time and authorizes the Assistant Commissioner to charge the cost of such petitions and/or other fees due in connection with the filing of this document to **Deposit Account No. 03-1952** referencing docket no. 509132000100. However, the Assistant Commissioner is not authorized to charge the cost of the issue fee to the Deposit Account.

Respectfully submitted,

Dated: November 1, 2002

By: _____

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VERSION WITH MARKINGS TO SHOW CHANGES MADE

In the Specification:

Please amend paragraph 24 on page 7 as follows:

Figure 4 illustrates the effect of the LXR pan-agonist Compound 1 on lipoprotein lipase (LPL) mRNA levels in wildtype, LXRα-/-, LXRβ-/-, and LXRαβ-/- mice. Compound 1 (10 mg/kg) was dosed daily for seven days by oral gavage. LPL levels were measured by quantitative PCR of total liver RNA. Data is expressed as fold induction by Compound 1 (+Compound 1/ Vehicle, [black]hatched bars). The value for vehicle treated mice in each group was set at 1.0 (white bars). Data is the average of four animals per group assayed in triplicate. *Signifies that the value is statistically different from the vehicle treated value within each genotype.

Please amend paragraph 25 on page 7 as follows:

Figure 5 illustrates the effect of the LXR pan-agonist Compound 1 on HDL cholesterol levels in wildtype, LXRα-/-, LXRβ-/-, and LXRαβ-/- mice. Compound 1 (10 mg/kg) was dosed daily for seven days by oral gavage. HDL levels were determined from plasma samples taken on day 7. Data presented is the average value derived from seven animals in each group except for LXRα-/-/C57BL/6 which is the average of six animals. (+Compound 1/Vehicle, [black]hatched bars; vehicle only, white bars.) *Signifies that the value is statistically different from the vehicle treated value within each genotype.

Please amend paragraph 26 on page 8 as follows:

Figure 6 illustrates the effect of the LXR pan-agonist Compound 1 on CYP7a mRNA levels in wildtype, LXRα-/-, LXRβ-/-, and LXRαβ-/- mice. Compound 1 (10 mg/kg) was dosed daily for seven days by oral gavage. CYP7a levels were measured by quantitative PCR of total liver RNA. Data is expressed as fold induction by Compound 1 (+Compound 1 /Vehicle, [black]hatched bars). The value for vehicle treated mice in each group was set at 1.0 (white

bars). Data is the average of four animals per group assayed in triplicate. *Signifies that the value is statistically different from the vehicle treated value within each genotype.

Please amend paragraph 27 on page 8 as follows:

Figure 7 illustrates the effect of the LXR pan-agonist Compound 1 on dietary cholesterol absorption. Compound 1 (50 mg/kg) was dosed daily for seven days by oral gavage. Cholesterol absorption was than measured using the fecal extraction method. Data is expressed as the percentage of radiolabeled cholesterol that was absorbed and is the average of seven animals in each group. (+Compound 1/Vehicle, [black]hatched bars; vehicle only, white bars.) *Signifies that the value is statistically different from the vehicle treated control value.

Please amend paragraph 28 on page 8 as follows:

Figure 8 illustrates the effect of the LXR pan-agonist Compound 1 on ABCA1 mRNA levels in the intestines of wildtype, LXRα-/-, LXRβ-/-, and LXRαβ-/- mice. Compound 1 (10 mg/kg) was dosed daily for seven days by oral gavage. ABCA1 levels were measured by quantitative PCR of total intestinal mucosa RNA. Data is expressed as fold induction by Compound 1 (+Compound 1/Vehicle, [black]hatched bars). The value for vehicle treated mice in each group was set at 1.0 (white bars). Data is the average of four animals per group assayed in triplicate. *Signifies that the value is statistically different from the vehicle treated value within each genotype.

Please amend paragraph 29 on page 8 as follows:

Figure 9A [illustrates the effect of transplanting ApoE-/- mice with bone marrow from LXRαβ-/-. A) R]shows representative sudan IV stained *en face* aorta preparations from ApoE-/- mice following LXRαβ-/- bone marrow transplants. Atherosclerotic lesions stain red. [B)]Figure 9B illustrates the effects of LXRαβ-/- bone marrow transplants on ApoE-/- mice via [Q]quantitation of the surface area of aortas covered with lesions. Data is the average of six aortas for the ApoE-/- toApoE-/- group and seven aortas for the wildtype to ApoE-/- and

LXRαβ-/- to ApoE-/- groups. *Signifies that the value is statistically different from the ApoE-/- to ApoE-/- control bone marrow transplant value.

Please amend paragraph 30 on page 8 as follows:

Figure 10A [illustrates the effect of transplanting LDLR-/- mice with bone marrow from LXRαβ-/-. A) R]shows representative sudan IV stained *en face* aorta preparations from LDLR -/- mice following LXRαβ-/-bone marrow transplants. Atherosclerotic lesions stain red. [B)]Figure 10B illustrates the effect of LXRαβ-/-bone marrow transplants on LDLR-/- mice via [Q]quantitation of the surface area of aortas covered with lesions. Data is the average of seven aortas for the LDLR-/- to LDLR-/- group, 11 aortas in the wildtype to LDLR-/- group, and 12 aortas in the LXRαβ-/- to LDLR-/- group. *Signifies that the value is statistically different from the LDLR-/- to LDLR-/- control bone marrow transplant value.

Please amend paragraph 32 on page 9 as follows:

Figure 12A illustrates the effect of the LXR pan-agonist Compound 1 on ABCA1 [(A) and ABCG1 (B)] mRNA levels in peritoneal macrophages isolated from mixed wildtype, LXRα-/- (C57BL/6), LXRβ-/-, and LXRαβ-/- mice. Peritoneal macrophages were cultured *in vitro* for 24 hours in the absence (white bars) or presence ([black]hatched bars) of 1.0 μM Compound 1, total RNA was isolated and the levels of the ABCA1 [and ABCG1] mRNA[s] were determined by quantitative PCR. Values reported are the averages of three samples for each group assayed in triplicate. Numbers above the [black]hatched bars are the values for the fold induction by Compound 1 (+Compound 1/Vehicle). Figure 12B illustrates the effect of the LXR pan-agonist Compound 1 on ABCG1 mRNA levels in peritoneal macrophages isolated from mixed wildtype, LXRα-/- (C57BL/6), LXRβ-/-, and LXRαβ-/- mice. Peritoneal macrophages were cultured *in vitro* for 24 hours in the absence (white bars) or presence (hatched bars) of 1.0 μM Compound 1, total RNA was isolated and the levels of the ABCG1 mRNA were determined by quantitative PCR. Values reported are the averages of three samples for each

group assayed in triplicate. Numbers above the hatched bars are the values for the fold induction by Compound 1 (+Compound 1/Vehicle).

Please amend paragraph 33 on page 9 as follows:

Figure 13 illustrates the effect of the LXR pan-agonist Compound 1 on cholesterol efflux in peritoneal macrophages isolated from wildtype (mixed and C57BL/6), LXRα-/- (C57BL/6), LXRβ-/-, and LXRαβ-/- mice. Peritoneal macrophages were cultured *in vitro* for 24 hours, cells were labeled with ^{14}C-cholesterol and cultured for an addition 24 hours in the absence (white bars) or presence ([black]hatched bars) of 1.0 μM Compound 1 to measure cholesterol efflux. Data is expressed as fold induction by Compound 1 (+Compound 1/Vehicle, [black]hatched bars). The value for vehicle treated cells in each group was set at 1.0 (white bars). Data is the average of three samples per group assayed in triplicate. *Signifies that the value is statistically different from the wildtype control value.